

Program/Abstract # 119**Wnt4a and Wnt11r coordinate branching morphogenesis of endodermal pouch epithelia by controlling cell migration and junctional ALCAM localization**Chong Pyo Choe^a, Megan Matsutani^a,Cecilia B. Moens^b, J. Gage Crump^a^aUniversity of Southern Cali Stem Cell & Regenerative Med, Los Angeles, CA, USA^bFred Hutchinson Cancer Research Center, Seattle, WA, USA

The pharyngeal pouches, evaginations of the foregut endoderm, are essential for segmentation of the developing vertebrate face. Here, we report a novel role of noncanonical (nc) Wnt signaling in regulating pouch formation in zebrafish. Using transgenic imaging approaches, we show that the pouches form by directed cell migration followed by cell rearrangements that organize endodermal cells into polarized bilayers. Next, we find that Wnt4a and Wnt11r are expressed in a segmental pattern in ectodermal and mesodermal cells, respectively, adjacent to fz8a-expressing pouch endodermal cells. Moreover, mutant and transgenic analyses show that Wnt4a/Wnt11r/Fz8a likely function through Dishevelled and the nc Wnt signaling to regulate pouch formation. By misexpressing dominant-negative and gain-of-function versions of nc Wnt pathway components in the endoderm, we find that Rac1 and JNK primarily regulate pouch cell migration, whereas Cdc42 primarily regulates pouch cell rearrangements via junctional localization of the immunoglobulin cell adhesion protein ALCAM. Interestingly, junctional ALCAM localization is dynamically regulated during pouch cell rearrangements and loss-of-function study suggests that ALCAM is not generally required for endodermal polarity but instead plays a regulatory role in re-establishment of epithelial polarity following pouch cell migration. In summary, our studies reveal that segmental Wnt expression in the ectoderm and mesoderm has a key role in vertebrate head segmentation. In addition, we propose that nc Wnt signaling has sequential roles in coordinating pouch formation, first in initiating cell migration that creates endodermal outpocketings and second in re-establishing epithelial polarity.

doi:[10.1016/j.ydbio.2011.05.143](https://doi.org/10.1016/j.ydbio.2011.05.143)**Program/Abstract # 120****Modeling lung branching morphogenesis via epithelial-mesenchymal interaction**Takashi Miura^a, Hiraga Kennichi^b, Tsuyoshi Hirashima^c^aKyoto Univ, Grad School Med Dept of Anatomy & Dev Biol, Kyoto, Japan^bKyoto, Japan^cKyoto University Graduate School of Medicine, Kyoto, Japan

Vertebrate lung forms branched structure during development. Numerous molecules are known to be involved in this process, but how the interaction of these molecules results in branching morphogenesis remains to be elucidated. In the previous study, we formulated a mathematical model that reproduces the formation of branches under in vitro condition without mesenchyme. However, since the epithelial-mesenchymal interaction is too complex to model, the mechanism in vivo remains to be elucidated. In the present study, we developed a reconstruction culture system that includes both epithelium and mesenchyme, and show that the epithelial explant in this culture system has an ability to generate branched structure. Under such a situation, we do not need to take organ shape into consideration and modeling is easier. In this culture system, expression of FGF10 is restricted to the region away from epithelial tissue. According to this information, we reduce the complex epithelial-mesenchymal interaction to two simple rules,

"FGF induces epithelial growth", and "Epithelium inhibits FGF production". There rules can be expressed as a combination of interface equation and convolution kernel. Numerical simulation of model reproduced the formation of branched structure with this model, and the characteristic size of the branched pattern can be obtained from mathematical analysis of the interface equation.

doi:[10.1016/j.ydbio.2011.05.144](https://doi.org/10.1016/j.ydbio.2011.05.144)**Program/Abstract # 121****Conditional embryonic over-expression of RAGE in the mouse lung diminishes pulmonary endothelium expression**

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Receptors for advanced glycation end-products (RAGE) are multi-ligand cell surface receptors prominently detected in lung epithelium. Previous experiments demonstrate that over-expression of RAGE in murine alveolar type (AT) II cells during embryogenesis causes severe lung hypoplasia and neonatal lethality. However, the effects of RAGE over-expression on adjacent endothelium are yet to be determined. Lung histology during developmental milestones revealed marked loss of parenchymal tissue beginning in the canalicular stage of lung development and continuing throughout the saccular period (embryonic day (E) 15.5–18.5). During these same periods, immunostaining for platelet endothelial cell adhesion molecule (PECAM) revealed a marginal decrease in microvascular endothelium prevalence in RAGE over-expressing mice compared to controls. In order to determine possible mechanisms of RAGE-mediated decreases in the derivation of endothelium, immunoblotting and RT-PCR for FoxM1, a key endothelium-specific transcription factor were performed. Experiments revealed RAGE over-expression by alveolar epithelium inhibits FoxM1, suggesting anomalous transcriptional control contributes to diminished endothelial cell prevalence in RAGE over-expressing mice. Additional research may reveal distinct RAGE-mediated pathways involved in vasculogenesis and angiogenesis necessary for the developmental derivation of normal pulmonary vasculature. Supported by the Flight Attendant's Medical Research Institute (FAMRI, PRR) and a BYU Mentoring Environment Grant (PRR).

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doi:[10.1016/j.ydbio.2011.05.146](https://doi.org/10.1016/j.ydbio.2011.05.146)**Program/Abstract # 123****Increased MMP-9 activity in mice that over-express RAGE in alveolar epithelium destabilizes the basement membrane by degrading collagen type IV**

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Background and rationale: RAGE, a receptor that binds multiple ligands, causes severe lung hypoplasia when over-expressed during embryogenesis. Destabilization of the basement membrane in the